



**Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register findings from a cohort sample**

Nissen, Judith; Powell, Shelagh; Koch, Susanne V.; Crowley, James J.; Matthiesen, Manuel; Grice, Dorothy E.; Thomsen, Per H.; Parner, E.

*Published in:*  
BMJ Open

*DOI:*  
[10.1136/bmjopen-2017-017172](https://doi.org/10.1136/bmjopen-2017-017172)

*Publication date:*  
2017

*Document version*  
Publisher's PDF, also known as Version of record

*Document license:*  
[CC BY-NC](#)

*Citation for published version (APA):*  
Nissen, J., Powell, S., Koch, S. V., Crowley, J. J., Matthiesen, M., Grice, D. E., Thomsen, P. H., & Parner, E. (2017). Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample. *BMJ Open*, 7(9), [e017172]. <https://doi.org/10.1136/bmjopen-2017-017172>

# BMJ Open Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample

Judith Nissen,<sup>1</sup> Shelagh Powell,<sup>1</sup> Susanne V Koch,<sup>2</sup> James J Crowley,<sup>3,4,5</sup> Manuel Matthiesen,<sup>4,5,6,7</sup> Dorothy E Grice,<sup>8,9</sup> Per H Thomsen,<sup>1</sup> E Parner<sup>10</sup>

**To cite:** Nissen J, Powell S, Koch SV, *et al.* Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample. *BMJ Open* 2017;7:e017172. doi:10.1136/bmjopen-2017-017172

► Prepublication history and additional material for this paper are available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2017-017172>).

Received 7 April 2017

Revised 8 June 2017

Accepted 4 July 2017

## ABSTRACT

**Objectives** Employing national registers for research purposes depends on a high diagnostic validity. The aim of the present study was to examine the diagnostic validity of recorded diagnoses of early-onset obsessive-compulsive disorder (OCD) in the Danish Psychiatric Central Register (DPCR).

**Design** Review of patient journals selected randomly through the DPCR.

**Method** One hundred cases of OCD were randomly selected from DPCR. Using a predefined coding scheme based on the Children's Yale Brown Obsessive Compulsive Scale (CYBOCS), experienced research nurse or child and adolescent psychiatrists assessed each journal to determine the presence/absence of OCD diagnostic criteria. The detailed assessments were reviewed by two senior child and adolescent psychiatrists to determine if diagnostic criteria were met.

**Primary outcome measurements** Positive predictive value (PPV) was used as the primary outcome measurement.

**Results** A total of 3462 children/adolescents received an OCD diagnosis as the main diagnosis between 1 January 1995 and 31 December 2015. The average age at diagnosis was 13.21±2.89 years. The most frequent registered OCD subcode was the combined diagnosis DF42.2. Of the 100 cases we examined, 35 had at least one registered comorbidity. For OCD, the PPV was good (PPV 0.85). Excluding journals with insufficient information, the PPV was 0.96. For the subcode F42.2 the PPV was 0.77. The inter-rater reliability was 0.94. The presence of the CYBOCS in the journal significantly increased the PPV for the OCD diagnosis altogether and for the subcode DF42.2.

**Conclusion** The validity and reliability of International Classification of Disease 10th revision codes for OCD in the DPCR is generally high. The subcodes for predominant obsessions/predominant compulsions are less certain and should be used with caution. The results apply for both children and adolescents and for both older and more recent cases. Altogether, the study suggests that there is a high validity of the OCD diagnosis in the Danish National Registers.

## INTRODUCTION

Obsessive compulsive disorder (OCD) is a common psychiatric disorder with an

## Strengths and limitations of this study

- The cases were randomly selected from all regions of Denmark to ensure a national representation.
- The patient journals were reviewed in accordance with a predefined scheme based on the Children's Yale Brown Obsessive Compulsive Scale ensuring a comparable evaluation across the different regions.
- Each patient scheme was independently assessed by two senior child and adolescent psychiatrists to ensure diagnostic accuracy. The inter-rater reliability was excellent.
- Important limitations include that the reviewers were not blinded for the diagnoses and the study did not include a control group. As such, it was not possible to define negative predictive value, sensitivity or specificity.

estimated prevalence of 1%–2%.<sup>1</sup> The disorder is characterised by intrusive, unwanted thoughts (obsessions) and repetitive ritualistic behaviours (compulsions). Approximately 50%–60% of the patients with OCD have an age of onset in childhood or adolescence.<sup>1</sup> Many individuals affected by OCD also have other psychiatric comorbidities, the symptoms of which may appear similar to the obsessions and compulsions of OCD. These include tics/Tourette syndrome, autism spectrum disorders (ASD) and other anxiety disorders. Furthermore, disorders such as schizophrenia may present with OC symptoms, which may not meet OCD criteria, but have similar characteristics as compulsions.<sup>1–4</sup>

For clinical purposes, an accurate diagnosis is critical since it guides treatment decisions. Likewise, for research purposes a correct diagnosis constitutes the foundation for valid and conclusive results that can be used to ensure a better understanding of the disorder concerning both the aetiology, the



CrossMark

For numbered affiliations see end of article.

## Correspondence to

Dr Judith Nissen;  
[judiniss@rm.dk](mailto:judiniss@rm.dk)

clinical presentation, treatment and the course of the disorder.

The Danish Psychiatric Central Register (DPCR) was established in 1969 as a nationwide electronic register of data regarding inpatient contacts for all Danish citizens, coded through a unique personal identification number assigned at birth. The DPCR was expanded in 1995 to include data from all outpatient contacts. The register is a longitudinal record with ongoing electronic registration of patients examined and/or treated at all psychiatric departments in Denmark.<sup>5</sup> Since 1995, the DPCR has been closely associated with the National Patient Register (LPR). The LPR was established in 1977 and contains information about inpatient admissions, and since 1995, both outpatients and emergency department visits. The information recorded in the registers is provided by clinicians from the relevant somatic and psychiatric wards. Since 1994, all diagnoses in the DPCR are recorded in accordance with the International Classification of Diseases 10th revision (WHO, ICD-10).

The DPCR and LPR contain important information concerning psychiatric and somatic diagnoses, length of hospital admittance and rehospitalisations. The registers are thus important for general health surveillance, including the frequency of illnesses and treatments, and they are used in economic decisions made by the health authorities. Furthermore, the registers form the basis for quality assurance in the health services.

Beyond health surveillance, the Danish registers are widely used in research. The focus of the register-based research has varied considerably. For example, prior population-based register studies on OCD and related disorders in Denmark have helped to identify key risk factors. In a three-generation study, Steinhausen *et al* showed that the occurrence of OCD, but also tic disorders, affective disorders and anxiety disorders in first-degree relatives increased the risk of OCD in the case proband. Furthermore, the risk of OCD was associated with maternal age and male sex.<sup>6</sup> Likewise, Browne *et al*<sup>7</sup> showed a clustering of Tourette syndrome and OCD in families indicating a significant familial recurrence including a cross-disorder risk. Meier *et al* examined OCD as a risk factor of a lifetime diagnosis of schizophrenia or a schizophrenia spectrum disorder. The risk was shown to be increased.<sup>8</sup> An additional study analysed all first admissions of OCD based on ICD-8 for diagnostic stability. About half of first-admission cases diagnosed with OCD kept OCD as a main diagnosis.<sup>9</sup>

The DPCR has furthermore been employed to ascertain other psychiatric diagnoses and afterwards combine diagnoses with information from other registers. In schizophrenia, Rajkumar *et al*<sup>10</sup> used Danish national registers to demonstrate that schizophrenia is associated with a high risk for diabetes and that the risk is further increased by both first-generation and second-generation antipsychotics. Recently, the registers were used as a basis for genetic/biomarker studies. For example, in schizophrenia, Laursen *et al*<sup>11</sup> examined the association

between an increased polygenic liability and the risk of dying early or attempting suicide. In ASD, Robinson *et al*<sup>12</sup> found genome-wide genetic links between ASD cases identified through the registers and typical variation in social behaviour and adaptive functioning. Thus, a broad variety of essential knowledge on OCD and other psychiatric disorders depends on the diagnostic validity of the registers.

Systematic studies measuring the validity of certain psychiatric diagnoses in Scandinavia have been published. In schizophrenia, Uggerby *et al*<sup>13</sup> reviewed case records for a random sample of 291 Danish patients with a first-time diagnosis of schizophrenia and showed a validity of 89.7%. In depression, Bock *et al*<sup>14</sup> examined records of 399 Danish patients with a registered diagnosis of a single depressive episode and found a validity of 75.4% (82.8% for a severe episode, 76.0% for moderate and 65.2% for mild). The validity of childhood autism diagnoses in Denmark was estimated at 94%<sup>15</sup> and similar estimates were found in Sweden.<sup>16</sup> In Sweden, Ruck *et al*<sup>17</sup> examined the validity and reliability of chronic tic and OCD diagnoses in the Swedish National Patient Register. They showed a high positive predictive value (PPV >0.90) for all ICD tic diagnoses (PPV 86%–97%) and ICD-10 OCD diagnoses (PPV 91%–96%). Finally, in Finland, Leivonen *et al*<sup>18</sup> demonstrated that the validity of diagnosed Tourette syndrome and other tic disorders exceeds 90%.

To our knowledge, there are no systematic studies validating childhood/adolescent OCD diagnoses in Danish registers. The aim of the present study was therefore to validate the diagnoses of early-onset OCD in the DPCR.

## METHODS

The study was approved by the Danish Data Protection Agency (J.nr. 2015-41-3999) and the National Board of Health (3-3013-1180/1: 19/10 2015).

### Case identification

We identified all newly diagnosed cases of OCD in children and adolescents (aged 0–17 years) as per documentation in the DPCR between 1 January 1995 and 31 December 2015. The following ICD-10 codes were used for main diagnoses: DF42.0 (predominantly obsessions), DF42.1 (predominantly compulsions) and DF42.2 (both obsessions and compulsions present). The DPCR included cases from all regions of Denmark and included both inpatient and outpatient contacts.

### Procedure

We requested personal identification numbers from all cases fulfilling the inclusion criteria mentioned above. After receiving these, the associated register data were grouped in relation to the Danish Children and Adolescent Psychiatric Hospitals representing each of the five regions of Denmark. From each region, 30–40 cases were randomly chosen for further review. From each 5-year period (1995–1999, 2000–2004, 2005–2009 and

2010–2015), at least five patients with a primary OCD diagnosis in the DPCR were included.

### File recording and review

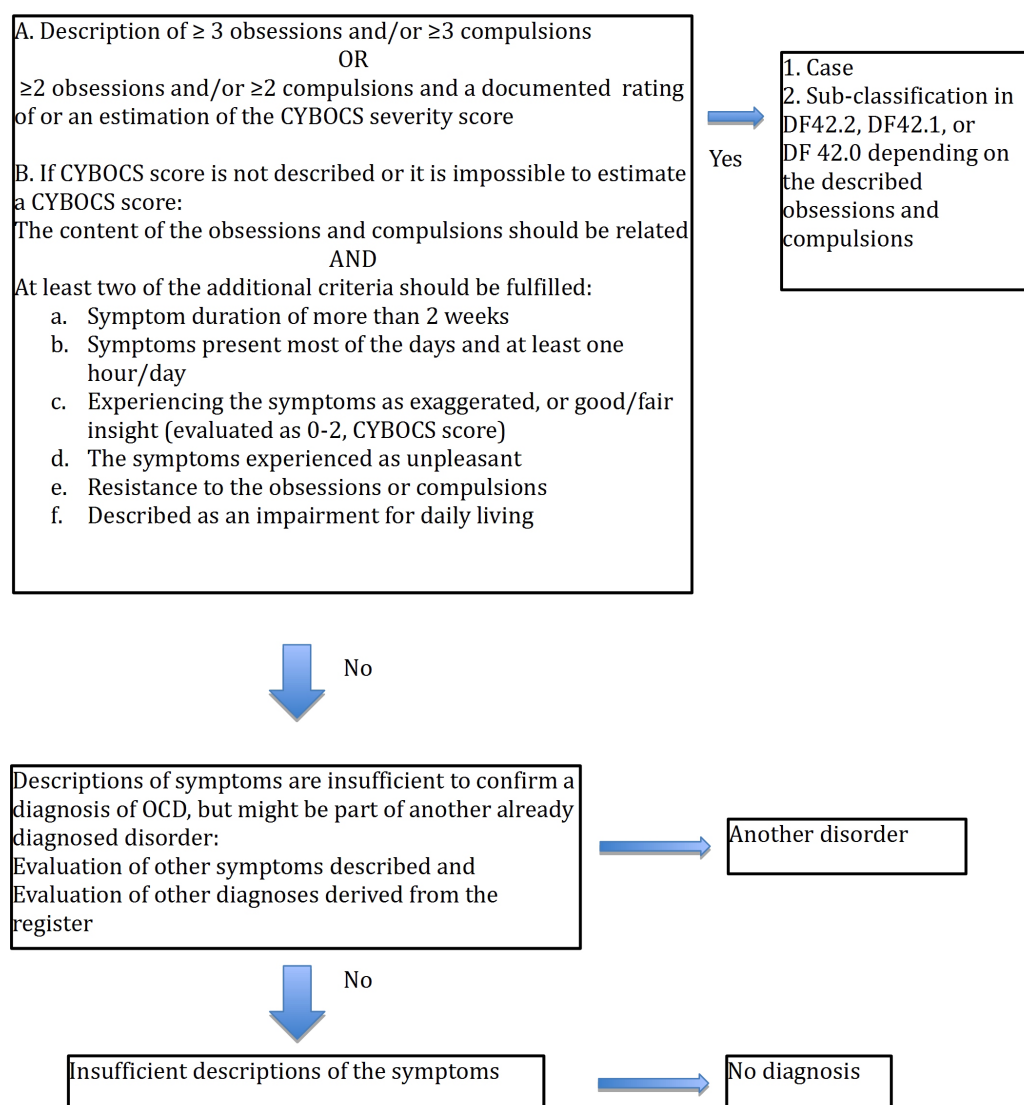
In each region, the patient journals were obtained from at least 20 patients on the sample list. In each patient file, the section describing the first OCD diagnosis was carefully recorded using a predefined coding scheme based on the ICD-10 criteria and DSM-IV-TR criteria for OCD (the predefined coding scheme is available as online supplemental data). The coding scheme included three main sections. Section 1 coded demographic information concerning the specific region, hospital and patient (including gender and age). Section 2 coded specific information about OCD including age of the first OCD symptoms and based on the CYBOCS, information concerning the presence or absence of specific obsessions and compulsions, and the described or estimated CYBOCS score. Section 2 also included questions concerning the duration of the OCD symptoms, insight

in the disorder, functional impairment, the resistance against OCD symptoms, and the control over OCD symptoms (rated as 0–4 as described in the CYBOCS). Section 3 coded the occurrence of symptoms found in other psychiatric disorders (eg, Tourette disorder, ASD, anxiety disorders, and mood disorders) to determine if overlapping symptoms were present. Chart assessments were performed by a psychiatric research nurse or by child and adolescent psychiatrists. To determine the final case status, the detailed recordings were reviewed by two experienced child and adolescent psychiatrists (JBN, SP). The final evaluation was based on the flowchart shown in figure 1.

The reviewers were blind to the OCD subcodes given in the psychiatric register.

### Statistical analyses

The PPV and the corresponding 95% CI were calculated using the binomial model. The PPV describes the correctly diagnosed cases divided by the sum of true-positive and



**Figure 1** Procedure for determining the final OCD study diagnosis. CYBOCS, Children's Yale Brown Obsessive Compulsive Scale; OCD, obsessive-compulsive disorder.



**Table 1** The number of newly diagnosed child and adolescent obsessive-compulsive disorder cases (0–17 years) found in the Danish Psychiatric Central Register between 1 January 1995 and 31 December 2015 (by sex, mean age at diagnosis and the five regions of Denmark)

Region of Denmark	Female N (%) (age±SD)	Male N (age±SD)
Region Capital	366 (56%) (13.01±2.93)	288 (12.53±3.08)
Region South	147 (58%) (13.06±3.00)	108 (12.72±2.99)
Region Central	568 (55%) (13.52±2.76)	477 (13.33±2.80)
Region North	128 (54%) (13.37±2.67)	107 (13.30±2.75)
Region Zealand	222 (56%) (13.83±2.79)	181 (13.19±3.15)

false-positive cases. The inter-rater reliability between the two specialists was calculated by dividing the number of identical evaluations with the total number of cases. A t-test was used to identify statistically significant differences of continuous outcome between diagnostic groups, and robustness of the t-test to departures of normality was assessed using the bootstrap procedure. Fisher's exact test was used to examine statistically significant differences between categorical outcomes. p Values <0.05 were considered statistical significant. SPSS Statistics V.10 was used for all calculations.

## RESULTS

### The main register-based sample

Throughout Denmark, a total of 3462 children and adolescents aged 0–17 years received an OCD diagnosis as the main diagnosis in the time period between 1 January 1995 and 31 December 2015. The average age (±SD) at diagnosis was 13.21±2.89 years and the number of females was 1905 (55%) (13.40±2.85 years) and of males 1557 (45%) (12.98±2.92 years). The distribution of registered

OCD cases in relation to the regions of the participating children and adolescents psychiatric hospital departments is shown in [table 1](#).

### Description of the included cases

A total of 100 journals were evaluated in accordance with the predefined coding scheme. A detailed description of the included cases is shown in [table 2](#). In total and for each of the five included regions, the most frequent registered OCD subcode was the combined diagnosis DF42.2. The occurrence of predominantly obsessions (DF42.0) or predominantly compulsions (DF42.1) were comparable. The average age for the first OCD diagnosis was comparable for the five included regions of Denmark. Of these 100 OCD cases, 35 had at least one other psychiatric diagnosis in the DPCR (21 with one comorbidity, 11 with two comorbidities and the remaining patients with three comorbidities). The most frequent co-occurring diagnoses were anxiety disorders (n=6), specific or pervasive developmental disorders (n=10), attention deficit hyperactivity disorder/attention deficit disorder (n=5) and tic disorders (n=7). Of note, several journals also listed comorbid depressive symptoms, but not a formal diagnosis of major depressive disorder (data not shown).

### Validity of OCD diagnosis

Of the 100 journals, OCD diagnoses could be confirmed in 85 journals corresponding to an overall PPV for OCD of 0.85 (95% CI: 0.76 to 0.91). Eleven journals that had an OCD diagnosis assigned did not contain sufficient information via our coding scheme to confirm or exclude the occurrence of OCD obsessions or compulsions. If these journals were excluded from further analyses, the PPV for OCD would be 85/89 or 0.96 (95% CI: 0.89 to 0.99). Among the remaining 89 patients for whom we had sufficient information, 85 were rated as true-positive cases based on the documented OCD symptoms, the severity and duration of symptoms, the patient's insight and the presence of comorbidity. The remaining four patients were determined to be false-positive cases because the OCD diagnosis could not be confirmed through the coding scheme. Based on the documented symptoms,

**Table 2** Characteristics of 100 newly diagnosed, early-onset obsessive-compulsive disorder cases randomly chosen from the Danish Psychiatric Central Register for examination of diagnostic validity

Region of Denmark	Number of records examined (%)	Age (mean±SD)	Female/male	Register* diagnosis DF42.0 (%)	Register diagnosis DF42.1 (%)	Register diagnosis DF42.2 (%)
Region Capital	24 (24)	11.70±3.00	11/13	29.2	20.8	50.0
Region South	20 (20)	12.53±2.86	9/11	5.0	25.0	70.0
Region Central	20 (20)	11.30±2.74	12/8	15.0	10.0	75.0
Region North	20 (20)	12.25±2.02	12/8	15.0	5.0	80.0
Region Zealand	16 (16)	12.25±3.30	6/10	18.8	31.3	50.0
Total	100	11.98±2.78	50/50	17.0	18.0	65.0

Diagnoses are recorded using the International Classification of Diseases 10th revision (WHO, ICD-10) criteria.

\*Danish Psychiatric Central Register.

**Table 3** PPV (95% CI) of OCD codes in relation to the date and age at the first OCD diagnosis, sex and the inclusion of CYBOCS

Criteria	OCD (all diagnoses) PPV (95% CI)	DF42.2 PPV (95% CI)
Diagnosed before 2000	0.74 (0.52 to 0.90) (n=23)	0.64 (0.31 to 0.89) (n=11)
Diagnosed after 2000	0.88 (0.79 to 0.95) (n=77)	0.80 (0.66 to 0.89) (n=54)
	p=0.09	p=0.26
Diagnosed before age 12	0.83 (0.69 to 0.93) (n=42)	0.71 (0.51 to 0.87) (n=28)
Diagnosed after age 12	0.86 (0.75 to 0.94) (n=58)	0.81 (0.65 to 0.92) (n=37)
	p=0.69	p=0.37
CYBOCS not performed	0.75 (0.62 to 0.86) (n=56)	0.59 (0.39 to 0.76) (n=29)
CYBOCS performed	0.98 (0.88 to 1.00) (n=44)	0.92 (0.78 to 0.98) (n=36)
	p=0.001*	p=0.001*
Female	0.88 (0.76 to 0.95) (n=50)	0.88 (0.72 to 0.97) (n=33)
Male	0.82 (0.69 to 0.91) (n=50)	0.66 (0.47 to 0.81) (n=32)
	p=0.41	p=0.03*
All cases included	0.85 (0.76 to 0.91)	0.77 (0.65 to 0.86)

\*p<0.05 statistically significant difference.

CYBOCS, Children's Yale Brown Obsessive Compulsive Scale; OCD, obsessive-compulsive disorder; PPV, positive predictive value.

these four patients were best characterised as having a tic disorder (2), a separation anxiety disorder (1) or an eating disorder (1).

### Validity and reliability of OCD subcodes

Further examination of individual subcodes of the 85 true-positive OCD cases showed that 64 cases had both obsessions and compulsions documented corresponding to a PPV for DF42.2 of 0.77 (95% CI: 0.65 to 0.86), 15 journals were found to have documentation of only compulsions (PPV 0.28, 95% CI: 0.10 to 0.53) and six journals documented only obsessions (PPV 0.18, 95% CI: 0.04 to 0.43). The inter-rater reliability on the OCD subcodes altogether (DF42.2, DF42.1 and DF42.0) was 0.94.

Next, PPVs were analysed in relation to age of diagnosis (before or after age 12), sex, the diagnosis date (before or after 2000) and whether or not the clinician had administered the CYBOCS<sup>19 20</sup> (see table 3). The date of diagnosis or age at first OCD diagnosis showed no difference in the PPV for OCD or for DF42.2. The use of the CYBOCS, however, significantly increased the PPV of an OCD diagnosis and of the subcode DF42.2. Furthermore, the diagnosis of female cases with DF42.2 showed a significantly better PPV than a diagnosis of DF42.2 in male cases.

### DISCUSSION

National registers provide important information concerning psychiatric and somatic diagnoses, and are thus important for general health surveillance and a wide range of research studies. Establishing the diagnostic validity of specific disorders is thus an important foundation for subsequent analysis and interpretation of register clinical data.

The present study is the first to report on the diagnostic validity of OCD diagnoses in the DPCR.<sup>5</sup> Overall, the validity of the ICD-10 codes was rated as good (PPV=0.85), when rating the overall occurrence of OCD. Excluding the journals with insufficient recorded information yielded an excellent PPV (0.96). This is consistent with the results from a recent Swedish study examining the ICD-10 codes for OCD showing an excellent validity.<sup>17</sup> Most of the 11 files that were excluded in this study gave only limited descriptions of the experienced obsessions and compulsions. Furthermore, they lacked information concerning the duration of the symptoms, insight, discomfort and the resistance towards the thoughts and rituals and the experienced control. The documented information was rated as too limited to make a valid assessment of the OCD diagnosis.

Equally good validity was seen in journals from both before and after 2000, and for children and adolescents. Inclusion of the CYBOCS in the clinical examination showed a significantly higher PPV in our study. The CYBOCS is a semi-structured questionnaire that ascertains detailed OCD information including how much time is spent engaged in symptoms, level of distress and interference, ability to resist and degree of control over symptoms. There are also questions related to insight, pathological doubting, avoidance and other symptoms commonly found in OCD. The detailed information from the CYBOCS therefore increases the certainty of the diagnoses rendering the questionnaire important to include in clinical work.

In the present study, we also examined the validity of ICD-10 subcodes of OCD. The ICD-10 subcode DF42.2 showed good validity (PPV 0.77), whereas the subcodes

DF42.1 and especially DF42.0 were associated with a higher number of false-negative (ie, the patient journals contained descriptions of obsessions or compulsions although the diagnoses were registered otherwise). Overall, we found that the OCD combined subtype showed the highest validity and our results suggest caution when relaying on OCD subdiagnoses. Documented use of the CYBOCS increased the validity for the subcode DF42.2 significantly.

In conclusion, this study supports the validity of OCD diagnoses, particularly DF42.2, in the DPCR, opening the way for future studies of OCD based on DPCR information. The use of the CYBOCS is recommended to improve assessments.

### Strengths and limitations

The strength of this study is the random selection of the recorded journals from all individuals hospitalised for OCD throughout Denmark. The journals were evaluated by a skilled research nurse or child and adolescent psychiatrists in accordance with a predefined coding scheme, which was, in turn, evaluated by two experienced child and adolescent psychiatrists using ICD-10 criteria for OCD. The inter-rater reliability was excellent. The main limitation of our study is the lack of control groups. This hinders the definition of the negative predictive value, sensitivity and specificity of the codes. Furthermore, the lack of control groups also increases the risk of over-confirming OCD diagnoses. Another important limitation is that the evaluation was not performed as a structured clinical examination by an expert, since this would most likely increase the validity of the description and interpretation of the symptoms. This would be the ideal procedure. However, the procedure would not be possible because of temporal and ethical aspects, where historical cases might have overcome their symptoms or have different symptoms than at the time of diagnosis.

### CONCLUSIONS

The validity of the OCD diagnosis in the Danish clinical register is very good. Thus, the registers are an important resource for future epidemiological and genetic studies of OCD.

#### Author affiliations

<sup>1</sup>Center for Child and Adolescent Psychiatry, Aarhus University Hospital Risskov, Risskov, Denmark

<sup>2</sup>Mental Health Centre for Child and Adolescent Psychiatry, Institute of Health Sciences, University of Copenhagen, Copenhagen, Denmark

<sup>3</sup>Department of Genetics and Psychiatry, University of North Carolina, Chapel Hill, USA

<sup>4</sup>Department of Clinical Neuroscience, Centre for Psychiatry Research, Karolinska Institute, Stockholm, Sweden

<sup>5</sup>Stockholm Health Care Services, Stockholm County Council, Stockholm, Sweden

<sup>6</sup>The Lundbeck Foundation Initiative for Integrative Psychiatric Research, Aarhus, Denmark

<sup>7</sup>Department of Biomedicine and Centre for Integrative Sequencing (iSEQ), Aarhus University, Aarhus, Denmark

<sup>8</sup>Division of Tics, Obsessive-Compulsive Disorder (OCD) and Related Disorders, Icahn School of Medicine at Mount Sinai, New York, USA

<sup>9</sup>Friedman Brain Institute and Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, USA

<sup>10</sup>Section of Biostatistics, Department of Public Health, Aarhus University, Aarhus, Denmark

**Acknowledgements** We wish to thank Sanne Rosenfeldt Fald Hansen, Region of Southern Denmark, Kirsten Krarup Keller, Region of Northern Denmark, Ida Karina Jøhnik, Region Zealand for their great work in evaluating the journals.

**Contributors** JN obtained funding, acquired the approvals, designed the study, acquired data, analysed data and wrote the first draft of the paper. SVK contributed to data acquisition and to drafting the manuscript. SP contributed to data analysis and inter-rater reliability JJC, MM, DEG and PHT contributed to the design of the study and drafting of the manuscript. EP contributed to data analysis and drafting the manuscript. All authors approved of the final version of the manuscript.

**Funding** JJC and MM were supported by NIH grant R01MH105500. DEG was supported in part by the Friedman Brain Institute and Mindich Child Health and Development Institute. JN was partly supported by The Lundbeck Foundation, grant number R185-2014-2486.

**Competing interests** None declared.

**Patient consent** Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

**Ethics approval** The Danish Data Protection Agency (J.nr. 2015-41-3999) and the National Board of Health (3-3013-1180/1: 19/10 2015).

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** No additional data available.

**Open Access** This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

### REFERENCES

1. Geller DA. Obsessive-compulsive and spectrum disorders in children and adolescents. *Psychiatr Clin North Am* 2006;29:353–70.
2. Horwath E, Weissman MM. The epidemiology and cross-national presentation of obsessive-compulsive disorder. *Psychiatr Clin North Am* 2000;23:493–507.
3. Oulis P, Konstantakopoulos G, Lykouras L, et al. Differential diagnosis of obsessive-compulsive symptoms from delusions in schizophrenia: a phenomenological approach. *World J Psychiatry* 2013;3:50–6.
4. Paula-Pérez I. Differential diagnosis between obsessive compulsive disorder and restrictive and repetitive behavioural patterns, activities and interests in autism spectrum disorders. *Rev Psiquiatr Salud Ment* 2013;6:178–86.
5. Mors O, Perto GP, Mortensen PB. The Danish Psychiatric Central Research Register. *Scand J Public Health* 2011;39(7 Suppl):54–7.
6. Steinhausen HC, Bisgaard C, Munk-Jørgensen P, et al. Family aggregation and risk factors of obsessive-compulsive disorders in a nationwide three-generation study. *Depress Anxiety* 2013;30:1177–84.
7. Browne HA, Hansen SN, Buxbaum JD, et al. Familial clustering of tic disorders and obsessive-compulsive disorder. *JAMA Psychiatry* 2015;72:359–66.
8. Meier SM, Petersen L, Pedersen MG, et al. Obsessive-compulsive disorder as a risk factor for schizophrenia: a nationwide study. *JAMA Psychiatry* 2014;71:1215–21.
9. Thomsen PH, Jensen J. Obsessive-compulsive disorder: admission patterns and diagnostic stability. A case-register study. *Acta Psychiatr Scand* 1994;90:19–24.
10. Rajkumar AP, Horsdal HT, Wimberley T, et al. Endogenous and Antipsychotic-Related Risks for Diabetes Mellitus in Young People With Schizophrenia: a Danish Population-Based Cohort Study. *Am J Psychiatry* 2017;174:686–94.

11. Laursen TM, Trabjerg BB, Mors O, *et al.* Association of the polygenic risk score for schizophrenia with mortality and suicidal behavior - A danish population-based study. *Schizophr Res* 2017;184:122–7.
12. Robinson EB, St Pourcain B, Anttila V, *et al.* Genetic risk for autism spectrum disorders and neuropsychiatric variation in the general population. *Nat Genet* 2016;48:552–5.
13. Uggerby P, Østergaard SD, Røge R, *et al.* The validity of the schizophrenia diagnosis in the danish psychiatric Central Research Register is good. *Dan Med J* 2013;60:A4578.
14. Bock C, Bukh JD, Vinberg M, *et al.* Validity of the diagnosis of a single depressive episode in a case register. *Clin Pract Epidemiol Ment Health* 2009;5:4.
15. Lauritsen MB, Jørgensen M, Madsen KM, *et al.* Validity of childhood autism in the Danish Psychiatric Central Register: findings from a cohort sample born 1990–1999. *J Autism Dev Disord* 2010;40:139–48.
16. Gaugler T, Klei L, Sanders SJ, *et al.* Most genetic risk for autism resides with common variation. *Nat Genet* 2014;46:881–5.
17. Rück C, Larsson KJ, Lind K, *et al.* Validity and reliability of chronic tic disorder and obsessive-compulsive disorder diagnoses in the Swedish National Patient Register. *BMJ Open* 2015;5:e007520.
18. Leivonen S, Voutilainen A, Hinkka-Yli-Salomäki S, *et al.* A nationwide register study of the characteristics, incidence and validity of diagnosed Tourette syndrome and other tic disorders. *Acta Paediatr* 2014;103:984–90.
19. Scahill L, Riddle MA, McSwiggan-Hardin M, *et al.* Children's yale-brown obsessive compulsive scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;36:844–52.
20. Storch EA, Murphy TK, Geffken GR, *et al.* Psychometric evaluation of the Children's Yale-Brown Obsessive-Compulsive Scale. *Psychiatry Res* 2004;129:91–8.